June 1, 1997 (6:32PM)
Paul R. McCurdy, MD

DRAFT

Advisory Committee on Blood Safety and Availability

Minutes

First Meeting April 24-25, 1997

The Acting Executive Secretary called the first meeting of the Committee to order at 9:15 AM and introduced the 18 members, one consultant and six ex officio non-voting members representing six Federal Agencies (see attached list). The committee members were reminded of the information they were given by mail on ethical aspects of serving on this committee and were referred to the Office of General Council for clarification, further information, etc., as needed. Dr. Arthur Caplan then took the Chair.

In opening remarks, the Chairman noted the important advisory role of the Committee, the importance of the issues to be discussed at this meeting and the need for more than one meeting annually for the Committee to serve its purpose. He then introduced the Acting Assistant Secretary for Health (ASH).

The Acting ASH sketched the historical background of the Committee, stemming from a report commissioned by the Secretary of the Department of Health and Human Services (DHHS) from the Institute of Medicine (IOM) about the rise of AIDS in the early 80s and the infection of a large portion of patients with hemophilia by HIV contaminated clotting factor concentrates. To strengthen the decision-making process, the IOM report recommended the establishment of a Blood Safety Committee within DHHS under the Department's lead blood safety director (ASH has been so designated) and of an outside advisory group to consider not only scientific issues but also consumer and societal factors as they compare risks and benefits of various actions and provide their advice.

This is the first meeting of that outside advisory group. She further outlined the scope of blood safety activities in the Department and then called upon Agency representatives to describe each individual agency's cooperative role.

The Centers for Disease Control and Prevention (CDC) is the Federal public health agency that works with state health officials to detect and investigate threats to public health. With substantial intramural epidemiologic and laboratory expertise, the CDC can provide a rapid response to perceived problems for both acute threats and long term studies. Key activities include surveillance, epidemiologic investigations of outbreaks from blood and blood products and the development of prevention and control strategies. They can also provide information as to supply and shortages of some products, e.g., gamma globulin, both non-specific and specific for certain organisms. There are seven sentinel sites around the US to provide early warning about emerging infections. The Committee is needed to provide wise counsel for making difficult decisions concerning blood safety in the midst of many societal issues. The CDC also hopes that the Committee will be helpful in identifying and implementing better ways of risk communication, both known and unknown.

The Food and Drug Administration (FDA) is charged with addressing safety and efficacy as they regulate blood and blood products, but the issue of how safe is safe enough is omnipresent. In particular, there are no drugs, biologics or devices that are 100 percent safe. Regulatory activity can be set at more than one level of safety, but each may have a different effect on supply. A proposal to test non-virally inactivated gamma globulin for hepatitis C virus (HCV) with a PCR-based procedure stimulated manufacturers to pull untested material from the market. This resulted in critical shortages of some products. This Committee will halp balance some of these competing priorities in the advice provided to the Department.

The blood safety role of the National Institutes of Health (NIH) and one of its constituent Institutes,

the National Heart, Lung, and Blood Institute (NHLBI) is to support research. Several studies to reduce the transmission of infectious diseases by blood transfusion and improve safety were cited as examples. A number of the research resources, past and present, developed under NHLBI support have been made available to answer current safety questions, including some involving emerging viruses. The NHLBI works closely with the FDA and the CDC in supplementing and complementing their activities with sponsored research.

Ms. Mary Gustafson (FDA) provided the statutory basis for the regulation of blood and blood products, beginning with Acts passed at the turn of the last century and progressing with amendments and court decisions to the present. She also discussed the regulation of blood centers vs transfusion services, devices vs drugs or biologics, intrastate vs interstate, etc. Most importantly, expected standards are the same, although the level and source of inspections and regulations may differ.

Dr. Paul Mied (summary mailed to members in advance) provided an overview of FDA policies for lookback involving various infectios agents, HIV, HBV (Hepatitis B Virus), HCV and HTLV (Human T-cell lymphotrophic virus). Lookback involves product retrieval, if any has been distributed but not used, and recipient notification. The most elaborately stated lookback rules are for HIV seroconverting donors. At issue is whether or not these other than product retrieval should be applied to other agents and if so, which ones. This discussion applied primarily to fresh blood products or components; plasma protein derivatives (e.g., clotting factor concentrates) are quite safe from enveloped viruses such as HCV because of the virus inactivation procedures used in their purification. There was also mention of reverse targeted lookback, defined as from an ascertained recipient seroconversion back to the donor and back again to other recipients.

Dr. Jay Hoofnagle (NIDDK) summarized current knowledge of the clinical features of hepatitis C. Its

most important feature is its tendency toward chronicity. Eighty-five or more percent of patients remain intermittently or continuously viremic and 60 percent have abnormal liver enzymes for prolonged periods. Although some patients with chronic hepatitis C develop cirrhosis -- one estimate is around 25 percent --, most do not. The virus itself is quite variable, posing potential problems for detection. Interferon is the only therapy available for HCV infection and its response rate is relatively low — 15-30 percent. Twelve months of therapy seems better than six.

Dr. Harold Margolis (CDC) emphasized that nearly all hepatitis C comes from parenteral exposure, transfusion or sharing of contaminated needles during drug use. He also discussed approaches to lookback, e.g., focused lookback from positive donors or a puch toward public and professional education re hepatitis C. More patients with hepatitis C were infected through shared needles than from transfusion, but by the time they are in treatment, they are already infected. There is little opportunity for prevention in drug users at this point.

Dr. Merlyn Sayers (Dallas) pointed out that some HCV infected blood donors were detected by surrogate tests, although there was no question of lookback. More infectious donors were screened out with the HCV antibody tests, however. He finished with a brief discussion of the inefficiency and costliness of attempting retrospective HCV-positive donor-directed lookback, commenting that such discussions in the past have been considered self-serving when given by blood bankers.

Dr. Steve Kleinman (AABB) commented during the Open Public Discussion (Attached).

Dr. Celso Bianco (ABC) commented during the Open Public Discussion (Attached).

Dr. Glenn Pierce (NHF) commented during the Open Public Discussion (Attached).

Edward Burke, a person with hemophilia, commented during the Open Public Discussion.

There was limited reference to lookback programs in Canada (varies from province to province), in Britain and in Australia. More information would be of interest. Similarly, there was no presentation about costs vs benefits of HCV lookback. To factor that into the discussion, more information would need to be made available. Other questions raised by the committee include: Morbidity and mortality data from HCV infection. Legal implications of notifying recipients of possible infections. How many blood recipients from several years ago are still alive? Is it appropriate to assume that a transfused patient with HCV got his/her infection from the transfusion?

At 5:15, the Committee recessed until 8:30 the following morning.
The Committee reassembled at 8:30 AM, April 25, 1997.

Dr. Thomas Zuck (Hoxworth Blood Center, Cincinnatti; temporarily at the NY Blood Center) gave an overview of the blood banking establishment and its multiple parts as it exists today in the US.

The Committee then revisited the hepatitis C lookback issue, first reviewing a series of questions posed by the PHS as options to be discussed and selected (Attached). The Committee was reluctant to be bound by yes-no answers to such questions, preferring instead more narrative opinions and perhaps a guidance document that would advise re policy. This would be "more of a framework, more of principles, more of points to consider, statements that might be supported by some rationale or explanation as part of how it (the ommittee) thinks it can be most useful." DHHS' prefers either a policy statement or something that can be readily turned into a policy statement on the lookback issue. There was considerable discussion on the need for education, both of patients and former patients and of physicians involved in the follow-up care of those patients. The lookback issue can also be divided by time: pre-1990, 1990-1997, and forward from now. Further, heavy

users may need to be dealt with differently than occasional users of blood.

After a brief break, two presentations on Creutzfeldt-Jakob Disease (CJD)(vide infra) and lunch, the Committee again revisited the HCV issue. Drs. John Penner and W. Keith Hoots presented draft policy statements concerning HCV lookback (Attached). During the discussion, it was suggested that a global public information effort be directed at subjects transfused both before 1990 and between 1990 and 1992 (the introduction of the second generation HCV antibody test and of a supplemental test). There was considerable discussion as to ways and means, with some emphasis that patients would be created — those found to harbor the HCV — and that some thought should be given as to how to deal with them. It was decided that these drafts would be the basis for further discussion and additional Committee education. At the next meeting (time TBD), the Committee would plan to finalize recommendations, using these documents as a start.

The Committee then turned to presentations on CJD. Dr. Paul Brown (NINDS, NIH) provided an overview of CJD and other transmissible spongiform encephalopathies (TSE). These disorders are transmissible, most notably by intracerebral injection, but occasionally, although inefficiently by parenteral injection. Transmission by blood transfusion theoretically can happen, but experimental data are limited. He described studies done with a mouse-adapted strain of CJD showing that plasma, buffy coat and cryoprecipitate can transmit by intracerebral injection. Additional studies are planned to determine if intravenous injection can transmit.

Dr. Robert Rowher (VAH, Baltimore) described studies with hamster-adapted scrapie that did suggest transmission by intravenous blood transfusion. Additional research is needed to confirm and study this further. He finished by suggesting, mathematically, that many if not most plasma pools contain plasma from individuals incubating CJD — the incubation period may be 20-40 years. If they are infectious during that time, most pools are so contaminated and have been for many

years.

Dr. Larry Schonberger (CDC) discussed the epidemiology of CJD, with particular regard to transmission by transfusion of blood or blood products. None of the studies, case control, general surveillance or death certificate review were able to identify blood transfusion as a risk factor for getting CJD. This included very recent studies of a group of patients with hemophilia who were treated nearly exclusively with cryoprecipitate from before 1970 to the mid-1980s.

Ms. Sullivan presented the (negative) results of Red Cross lookback to recipients of blood from donors who later came down with CJD.

Dr. Mark Weinstein presented the FDA's current and immediate past response to the CJD issue, including recall of products, etc. The recall policy, initial and revised, cut deeply into the supply of plasma protein derivatives, but is not known to have caused a patient-harming shortage.

During the Open Public Hearing, Dr. Glenn Pierce presented the CJD issue from the viewpoint of patients with hemophilia. Having been infected in the past with hepatitis and HIV, the hemophilia community as concerned that products used by them, made from pools of up to 60,000 donors, make them a bellweather of infectious agents in the blood supply. Lipid enveloped viruses are well destroyed by current treatment methods; non-lipid enveloped viruses and agents such as the one for CJD are not.

Dr. Peter Page (ARC, NHQ) discussed how multiple recalls have affected derivative supply and and manufacturer's costs. Shortages have not yet directly affected patients. Red Cross has lost derivatives worth more than $100 million.

Dr. Celso Bianco (NY Blood Center) made a presentation on behalf of America' Blood Centers, Mr. Bell on behalf of the International Plasma Products Industry Association (IPPIA) and Dr. Kleinman on behalf of the AABB (See Attached). The meeting concluded with a presentation from Ms. Angie Hendrickson, mother of a 14 year old with hemophilia A who has AIDS, HCV infection and has been afflicted with parvo virus infection. She reported CJD withdrawal notifications since 1994. She expressed concern about mixed messages, now and in the past, and pleaded for direct attention to blood safety.

Dr. Goosby closed the meeting with brief remarks.

COMMITTEE ROSTER

National Advisory Research Resources Council
NATIONAL CENTER FOR RESEARCH RESOURCES

CHAIRPERSON

VAITUKAITIS, JUDITH L., BS, MD 31-JAN-99
DIRECTOR
NATIONAL CENTER FOR RESEARCH RESOURCES
NATIONAL INSTITUTES OF HEALTH
9000 ROCKVILLE PIKE
BETHESDA, MD 20892

COLLINS, DELWOOD C., PHD, MS 31-JAN-01
PROFESSOR
DEPT FOR RESEARCH AND GRADUATE STUDIES
UNIVERSITY OF KENTUCKY MEDICAL CENTER
LEXINGTON, KY 40536-0305

DAVISSON, MURIEL T., PHD 31-JAN-01
SENIOR STAFF SCIENTIST/DIRECTOR
THE JACKSON LABORATORY
BAR HARBOR, ME 04609

FEIN, RASHI, PHD 31-JAN-99
PROFESSOR
DEPARTMENT OF SOCIAL MED & HEALTH POLICY
SCHOOL OF MEDICINE
HARVARD UNIVERSITY
BOSTON, MA 02115

GLUSKER, JENNY P., DPH 31-JAN-99
SENIOR MEMBER
THE FOX CHASE CANCER CENTER
PHILADELPHIA, PA 19111

HEARN, JOHN, PHD 31-JAN-99
PROFESSOR
ANU-RSBS
CANBERRA ACT 0200
AUSTRALIA

HO, CHIEN, PHD 31-JAN-02
PROFESSOR
DEPARTMENT OF BIOPHYSICAL CHEMISTRY
MELLON COLLEGE OF SCIENCE
CARNEGIE MELLON UNIVERSITY
PITTSBURGH, PA 15213

HODGSON, KEITH, PHD 31-JAN-00
PROFESSOR
DEPARTMENT OF CHEMISTRY
SCHOOL OF HUMANITIES & SCIENCES
STANFORD UNIVERSITY
STANFORD, CA 94305

JOHNS, MICHAEL, MD 31-JAN-02
EXEC VICE PRESIDENT FOR HEALTH AFFAIRS
ROBT. W. WOODRUFF HEALTH SCI CENTER
EMORY UNIVERSITY
ATLANTA, GA 30322

KATONA, PETER, BS, MS 31-JAN-01
EXECUTIVE VICE PRESIDENT
DEPT OF BIOMEDICAL ENGINEERING
THE WHITAKER FOUNDATION
ROSSLYN, VA 22209

KOHLER, PETER O., MD 31-JAN-02
PRESIDENT
OREGON HEALTH SCIENCES UNIVERSITY
PORTLAND, OR 97201-3098

KRANIAS, EVANGELIA G., PHD 31-JAN-02
PROFESSOR
DEPT. OF PHARMACOLOGY & CELL BIOPHYSCS
COLLEGE OF MEDICINE
CINCINNATI, OH 45267

MALDONADO, NORMAN, MD 31-JAN-00
PRESIDENT
OFFICE OF THE PRESIDENT
UNIVERSITY OF PUERTO RICO
RIO PIEDRAS, PR 00926

MORSE, DANIEL, PHD 31-JAN-00
PROFESSOR
MARINE BIOTECHNOLOGY CENTER
MARINE SCIENCE INSTITUTE
UNIVERSITY OF CA, SANTA BARBARA
SANTA BARBARA, CA 93106

NEW, MARIA I., MD 31-JAN-00
PROFESSOR AND CHAIR
DEPARTMENT OF PEDIATRICS
CORNELL MEDICAL COLLEGE
CORNELL UNIVERSITY MEDICAL CENTER
NEW YORK, NY 10021

POWELL, DOROTHY L., EDD 31-JAN-99
DEAN
COLLEGE OF NURSING
HOWARD UNIVERSITY
WASHINGTON, DC 20059

WILSON, JAMES, MD, PHD 31-JAN-99
DIRECTOR, INST FOR HUMAN GENE THERAPY
MOLECULAR AND CELLULAR ENGINEERING
SCHOOL OF MEDICINE
UNIVERSITY OF PENNSYLVANIA
PHILADELPHIA, PA 19104-4268

WILSON, DONALD E., AB, MD 31-JAN-01
DEAN
SCHOOL OF MEDICINE
UNIVERSITY OF MARYLAND
BALTIMORE, MD 21201

ZIMMET, SHEILA COHEN, JD 31-JAN-00
ASSOCIATE MEDICAL CENTER COUNSEL
MEDICAL CENTER LIBRARY
MEDICAL CENTER
GEORGETOWN UNIVERSITY
WASHINGTON, DC 20007

FALLON, MICHAEL T., DVM, PHD
CHIEF VETERINARY MEDICAL OFFICER
RESEARCH SERVICE 151V
ATLANTA VA MEDICAL CENTER
DECATUR, GA 30033

SHALALA, DONNA E., PHD
SECRETARY
DEPARTMENT OF HEALTH AND HUMAN SERVICES
WASHINGTON, DC 20201

EX OFFICIO

HYAMS, KENNETH CRAIG, BA, MD
HEAD
EPIDEMIOLOGY DIVISION
NAVAL MEDICAL RESEARCH INSTITUTE
ROCKVILLE, MD 20852

VARMUS, HAROLD E., MD
DIRECTOR
NATIONAL INSTITUTES OF HEALTH, PHS, DHHS
BETHESDA, MD 20892